REMARKS

Claims 1-33 and 49-51 are pending. Claims 1-12, 14-20, 22-33 and 50-51 are withdrawn without prejudice. Claims 34-49 are cancelled. New claims 52-61 have been added. Applicant expressly reserves the right to pursue the withdrawn subject matter in a further application that claims priority under 35 U.S.C. § 120 from this application.

Claims 13 and 21 are currently amended. Support for these amendments is found throughout the application as filed, for example see the claims as originally filed, and in the published specification, see page 5, paragraph [0078], page 6, paragraph [0090] and page 10, paragraph [0134]. Applicants submit that no new matter has been added as a result of these amendments. Upon entry of the amendments, claims 13, 21 and 52-61 will be pending. Applicants request entry of the amendments and reconsideration of the claims.

Objections

In response to the Examiner's objection to claim 4, a substitute Figure 4 wherein the X-axis is labeled is enclosed.

Rejections Under 35 U.S.C. § 112

Claims 13, 21, 24, and 51 stand rejected under 35 U.S.C. § 112 as non-enabled for the treatment of all TH2 associated diseases. However, the Examiner concedes the specification is enabled for TH2 associated diseases "including atopic dermatitis, allergic asthma and allergic rhinitis".

Applicants assert that withdrawal of claims 24 and 51, without prejudice, and amendment of claims 13 and 21 renders the rejection moot.

Rejections Under 35 U.S.C. § 102(b) and § 103(a)

Claims 1, 3-6, 13, 19, 21, 24, 27-28 and 31-33 stand rejected under 35 U.S.C. § 102(b) in view of Franco *el al.*, 1998 ("Franco"). The Examiner asserts that Franco "teach a method for reducing TH2 immune response to an antigen comprising administering the antigen via an oral route (i.e. in immunotherapeutic form) and

subsequently administering the antigen in CFA by a subcutaneous injection (i.e. in immunogenic form comprising a TH1 adjuvant)".

Claims 1, 3-6, 13, 19, 21, 24, 27-28, 31-33 and 51 also stand rejected under 35 U.S.C. § 103 in view of Franco, in view of US Patent Application Publication 2002/0173625 (" '625"). The Examiner asserts that while "Franco et al. do not teach administering the immunotherapeutic form of the antigen by a sublingual route...[t]he '625 publication teaches that administration by oral or sublingual routes is routinely used in immunotherapeutic treatments for allergy". Applicant traverses.

For at least the reasons set forth herein below, Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness under the requirements of 35 U.S.C. § 103(a). To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or **motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings** (*In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)). Second, there must be a **reasonable expectation of success**. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on Applicants' disclosure. Finally, the prior art reference (or references when combined) must teach or suggest **all the claim limitations**. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974).

Franco discloses a method for inducing oral tolerance towards an antigen in ***unsensitized*** mice comprising feeding OVA (OVA-DNP) for a number of days and subsequently immunizing the mice by subcutaneous administration of OVA-DNP in CFA (Complete Freund's Adjuvant). Accordingly, the immune system of the subject of the method of Franco is naïve, in that the individuals of Franco are not sensitized to the antigen prior to administration of the antigen. That is, since the individual is not sensitized to an antigen associated with a TH2-immune response (sensitization, at least in an experimental setting, requires pre-sensitization of the individual to the antigen) these individuals do not have "a TH2-associated disease", and are not in need of treatment for a TH2-associated disease, as required by the instant claims.

In contrast to the method of Franco, the methods of claims 13 and 21 require an individual be in need of treatment for a TH2-associated disease. Thus the individuals of claim 13 and 21 are sensitized to the antigen prior to treatment according to the methods of the present invention.

The specification teaches throughout that the present invention relates to individuals already sensitized to antigen and not unsensitized individuals. One embodiment of the invention relates to the sublingual administration of an antigen to desensitize an individual (page 7, paragraph [0100]). Accordingly, the individual must have been previously sensitized to the antigen. Furthermore, an experimental example presented in the specification describes the sensitization of mice to test the method of the invention (see Example 5). Moreover, the specification refers to treating an individual afflicted with TH1 or TH2-associated disease ("[o]nce an individual afflicted with a TH1 or TH2-associated disease has been diagnosed" (page 6, paragraph [0089])). As such, it is clear from the specification that the present invention is directed towards individuals sensitized to antigen and therefore in need of treatment for a TH2-associated disease.

Furthermore, treatment according to the method of the present invention results in the down regulation of the immune response to a specific antigen. See, for example, Figures 5-7 (Example 5), which show that individuals sensitized to OVA and then treated with multiple sublingual doses of OVA before being given an intraperitoneal injection of OVA or OVA and alum had significantly lower anti-OVA IgE antibody levels than individuals sensitized to OVA and then treated with PBS.

As detailed above, the individuals subject to the Franco method are not sensitized to antigen before commencement of the method, and as such the individuals cannot become ***desensitized***.

Individuals treated with the method of Franco show an increase in antibody levels after treatment (see Franco, for example, page 4, Figure 1). Accordingly, while the Examiner is correct in the assertion that Franco does disclose the administration of an antigen via an oral route and subsequent administration of the antigen with adjuvant via

subcutaneous injection, and that this method does superficially resemble the claimed methods, in view of the foregoing it is clear that Franco does not teach or suggest a method of down regulating an immune response in an individual sensitized to an antigen or an individual in need of treatment for a TH2- associated disease. Applicants also submit that there is no disclosure in '625 that cures the deficiencies of Franco.

In conclusion, neither of Franco or the '625 publication, either alone or in combination, teach or suggest "a method of treating a TH2-associated disease selected from the group consisting of allergic atopic disorders, allergic asthma, atopic dermatitis and allergic rhinitis, said method comprising:

i). administering orally to an individual in need thereof an effective amount of an antigen in immunotherapeutic form; and

ii). subsequently administering to the individual still under the effects of immunotherapy an effective amount of an immunomodifying agent comprising said antigen in immunogenic form and a TH2-adjuvant, wherein the antigen specific TH2 response in the individual is reduced relative to the specific TH2 response before administration of said immunomodifying agent" as required by claim 13.

Further, neither of Franco or the '625 publication, either alone or in combination, teach or suggest "a method of treating a TH2-associated disease selected from the group consisting of allergic atopic disorders, allergic asthma, atopic dermatitis and allergic rhinitis comprising:

iii). administering orally to an individual in need thereof an effective amount of an antigen in immunotherapeutic form, wherein the immune response to said disease is down regulated; and

iv). subsequently administering to the individual still under the effects of immunotherapy an effective amount of an immunomodifying agent comprising said antigen in immunogenic form and a TH2-adjuvant" as required by claim 21.

Accordingly, Applicants request reconsideration and withdrawal of the rejections.

Rejections Under 35 U.S.C. § 102(b)

Claims 1, 3-8, 10, 13, 19, 21, 24 and 27-29 stand rejected under 35 U.S.C. § 102(b) in view of Drachenburg et al., 2001 ("Drachenburg"). The Examiner asserts that Drachenburg "teach a method of immunotherapy for treating pollen specific allergy comprising administering low doses of pollen allergen and MPL adjuvant (i.e. "immunotherapeutic dose") followed by administration of high doses of pollen allergen and MPL adjuvant (i.e. an "immunogenic" form of the antigen comprising a TH1 adjuvant)". Applicants traverse the rejection.

For a prior art reference to anticipate a claimed invention, the prior art must teach ***each and every element*** of the claimed invention. *Lewmar Marine v. Barient*, 827 F.2d 744, 3 USPQ2d 1766 (Fed. Cir. 1987).

While Drachenberg discloses a traditional immunotherapy method, comprising a series of injections with antigen of increasing strength and an adjuvant, which may correspond to step (i) of claims 13 and 21, Drachenburg does not teach or suggest a subsequent step of "administering to the individual still under the effects of immunotherapy an effective amount of an immunomodifying agent comprising said antigen in immunogenic form and a TH2-adjuvant", as required by claim 13 and 21.

Further, Drachenburg only discloses the administration of the antigen with a TH1-adjuvant (MPL), and not a TH2-adjuvant. Thus, Drachenburg fails to teach this element of the claims as well.

In conclusion, Drachenburg does not teach or suggest "a method of treating a TH2-associated disease selected from the group consisting of allergic atopic disorders, allergic asthma, atopic dermatitis and allergic rhinitis, said method comprising:

v). administering orally to an individual in need thereof an effective amount of an antigen in immunotherapeutic form; and

vi). subsequently administering to the individual still under the effects of immunotherapy an effective amount of an immunomodifying agent comprising said antigen in immunogenic form and a TH2-adjuvant, wherein the antigen specific TH2

response in the individual is reduced relative to the specific TH2 response before administration of said immunomodifying agent" as required by claim 13.

Drachenburg also does not teach "a method of treating a TH2-associated disease selected from the group consisting of allergic atopic disorders, allergic asthma, atopic dermatitis and allergic rhinitis comprising:

vii). administering orally to an individual in need thereof an effective amount of an antigen in immunotherapeutic form, wherein the immune response to said disease is down regulated; and

viii). subsequently administering to the individual still under the effects of immunotherapy an effective amount of an immunomodifying agent comprising said antigen in immunogenic form and a TH2-adjuvant" as required by claim 21.

Accordingly, Applicants request that the rejection under § 102(b) be withdrawn.

In view of the foregoing, Applicant requests reconsideration and allowance of the pending claims.

For at least the foregoing reasons, each of the presently pending claims in this application is believed to be in condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue. Should any of the claims not be found to be in condition for allowance, the Examiner is requested to call Applicant's undersigned representative to discuss the application. Applicant thanks the Examiner in advance for this courtesy.

The Director is hereby authorized to charge or credit any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105, under Order No. 65138(53253).

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